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Analysis of the Duration of Efficacy of Botulinum Toxin Type B in Patients with Cervical Dystonia

M.F. Lew
University of Southern California, Los Angeles, California, USA

Background: Intramuscular injections of botulinum toxin are widely accepted as treatment of choice for cervical dystonia (CD). The toxin acts by blocking the release of acetylcholine at the neuromuscular junction, causing a dose-dependent reduction in muscle activity while producing a reversible paralysis at the site of injection. Because the effects are temporary, repeat injection is required periodically to prevent recurrence of symptoms. Botulinum toxin type B (BoNT-B; Myobloc) has been shown in clinical trials to significantly reduce pain and postural abnormalities while improving physical functioning and overall quality of life. Objective: To determine the duration of efficacy of BoNT-B (Myobloc) injected into patients with CD. Methods: Data on the duration of efficacy of BoNT-B were compiled and analyzed from two placebo-controlled trials and two open-label trials. In the placebo-controlled trials, 186 patients received a single injection of BoNT-B at a dose of 5000 U or 10,000 U divided among the affected neck muscles. Efficacy was assessed by the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)-Total Scores at Weeks 4, 8, 12, and 16. The first open-label trial included 145 patients and evaluated escalating doses of 10,000 U, 12,500 U, and 15,000 U. Each patient was initiated on 10,000 U and received the subsequent higher dose after returning to their baseline CD status. TWSTRS-Total Scores were assessed every 4 weeks. The second open-label extension trial included 427 patients. The study was opened to patients who had participated in eight previous BoNT-B clinical trials, as well as a small number of drug-naïve patients. Doses ranged from 2500 U to 25,000 U. The change in TWSTRS-Total Scores from baseline to Week 4 was used to assess the effectiveness of repeated doses of BoNT-B. Results: In the two placebo-controlled trials, the mean time to return to baseline CD status was 12 to 16 weeks in patients treated with BoNT-B. Compared with patients receiving placebo, patients treated with BoNT-B had a significantly longer duration of treatment effect ($P < 0.01$ in both studies). In the first open-label trial, the majority of patients (<70%) in each dosing phase returned to baseline CD status between 12 and 16 weeks. There was a trend toward higher doses maintaining a longer duration of effect than the lower dose. With the highest dose of 15,000 U, 1 patient continued to benefit from treatment for 48 weeks. In the second open-label extension trial, the mean time between treatments varied between 14 and 16 weeks for treatment sessions 1 through 9. Beginning with the tenth treatment, there was a noticeable decrease in the mean time period between treatments. The shorter mean time between treatments is likely due to the fact that enrollment for many patients was truncated when the sponsor ended the extension trial when BoNT-B was approved by the U.S. FDA and in Europe for the treatment of CD. Conclusion: Based on the results of two placebo-controlled clinical trials and two open-label trials, the duration of efficacy of BoNT-B in patients with CD is 12 to 16 weeks.